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Influence of Outdoor Air Quality on Maxillofacial Growth and Development

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LOMA LINDA UNIVERSITY
School of Dentistry
in conjunction with the
Faculty of Graduate Studies

The Influence of Outdoor Air Quality on Maxillofacial Growth and Development

by

Ryan Rudd

A thesis submitted in partial satisfaction of
the requirements for the degree
Master of Science in Orthodontics and Dentofacial Orthopedics

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August 2012

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Each person whose signature appears below certifies that this thesis in his/her opinion is adequate, in scope and quality, as a thesis for the degree Master of Science.

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I can't express how thankful I am to have gone through all of this with my wife Katie. You've supported our family through both dental school and this residency. I've never met anyone who serves others as fully as you. I know the sacrifices you've made to accommodate my time in school have been huge and I hope someday to make it all worthwhile. To our two year old daughter Audrey, thanks for pretty much being oblivious to anything going on for the past two years.

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ABBREVIATIONS

Caltrans	California Department of Transportation
EPDC	Expected Peak Daily Concentration
FA	Facial Axis
FD	Facial Depth
GAG	Glycosaminoglycan
GIS	Geographic Information Systems
IRB	Institutional Review Board
KDF	Kernel Density Function
LFH	Lower Face Height
LLU	Loma Linda University
MP	Mandibular Plane
N24HA	National 24-Hour Average
NAA	National Annual Average
NAAQS	National Ambient Air Quality Standards
NO_2	Nitrogen Dioxide
O_3	Ozone
PHI	Protected Health Information
$PM_{2.5}$	Particulate Matter less than 2.5 micrometers in aerodynamic diameter
PM_{10}	Particulate Matter less than 10 micrometers in aerodynamic diameter
RBF	Radial Basis Function
RD	Road Density
T1	Time One (initial/pretreatment) records

TFH	Total Face Height
TP	Proximity to Traffic
TRI	Toxic Release Inventory
UK	Universal Kriging
USC	University of Southern California
U.S. EPA	United States Environmental Protection Agency

ABSTRACT OF THE THESIS

The Influence of Outdoor Air Quality on Maxillofacial Growth and Development

by

Ryan Rudd

Master of Science in Orthodontics, School of Dentistry
Loma Linda University, September 2012
Dr. Joseph Caruso, Chairperson

Introduction: Mild to moderate deviations from normal facial types can significantly change orthodontic treatment modalities. Studies linking ambient air pollution with respiratory problems, as well as craniofacial morphology with respiratory problems are well established.[1-19] In this study we aimed to determine if there was a correlation between ambient air pollution and maxillofacial growth and development. We also wanted to determine if further research should be done in this area, and if so how can the study be improved.

Materials and Methods: We selected Santa Maria, CA and Upland, CA as sample areas due to their significant differences in air quality. Initial lateral cephalometric radiographs were collected from 400 patients in each area. The combined 800 subjects' addresses were geocoded and ambient air pollution exposure was calculated based on air quality statistics from the California Air Resources Board, Environmental Protection Agency and NAVTEQ. Vertical measurements of facial depth (FD), total face height (TFH), lower face height (LFH), facial axis (FA), and mandibular plane (MP) were made on the initial T1 lateral cephalometric radiographs.

Statistical Analysis: Spearman's rho was used to determine if an association existed between the pollution metrics and craniofacial outcome variables.

Results: At a statistically significant level, no association exists between the pollution metrics (TRI, RD, TP, O_3, $PM_{2.5}$NAA, $PM_{2.5}$N24HA) and the craniofacial measurements (FD, MP, FA, LFH, TFH). The air quality between Upland and Santa Maria did differ significantly for O_3, $PM_{2.5}$NAA, and $PM_{2.5}$N24HA.

Conclusions: Increased exposure to ambient air pollution did not seem to have an effect on the craniofacial morphology of our sample groups. We were unable to account for the many confounding variables, which may have hampered our ability to see any correlation. Future studies should attempt to incorporate dichotomous sampling areas and account for as many confounding variables as possible.

CHAPTER ONE

INTRODUCTION

Statement of Problem

Diagnosing and treatment planning an orthodontic case requires a thorough analysis of several factors, including characteristics of the patient's craniofacial morphology. Mild to moderate deviations from normal facial types can significantly change orthodontic treatment modalities. Extreme morphological variations often require surgical correction to obtain functional and esthetic goals. Understanding the etiology of these morphological differences could aid orthodontists treat and potentially even prevent unfavorable growth patterns derived from environmental factors.

The influence of environmental factors on the growth and development of children has been studied for many decades. Studies linking ambient air pollution with respiratory problems, as well as craniofacial morphology with respiratory problems are well established[1-19]. Kaplan[20] attempted to find a direct association between air pollution and several measurements of malocclusion. She was able to find a correlation with Molar Relation, but drew from a relatively homogenous sample group. Her sample measured a relatively large environmental group, but the vast majority of the patients came from areas with poor air quality.

The purposes of this study were twofold: First, to assess the association between ambient air pollution and craniofacial measurements within two sample groups from two

very different air pollution environments. Second, to determine if further research should be done in this area and if so what changes should be made.

Hypothesis

The null hypothesis in this study was: There is no association between exposure to ambient air pollution and skeletal measurements of the vertical dimension among adolescents in a clinical cohort from Santa Maria, CA and Upland, CA.

The alternative hypothesis was: There is a significant association between exposure to ambient air pollution and skeletal measurements of the vertical dimension among adolescents in a clinical cohort from Santa Maria, CA and Upland, CA.

CHAPTER TWO

REVIEW OF THE LITERATURE

The Etiology of Craniofacial Growth

The driving force behind the development of the craniofacial complex has long been debated. During the first half of the 20th century, the orthodontic profession predominantly believed in the genetic theory, which stated that craniofacial growth could not be altered and was genetically predetermined. Edward Angle was one of the key supporters of the genetic theory, which led to widespread acceptance in the orthodontic community. Scientifically, there has been support for the genetic theory in studies that noted similarities in malocclusion among monozygotic twins.[21] In 1960, Moss proposed the functional matrix hypothesis, stating that all skeletal structures grow in direct response to its extrinsic, epigenetic environment.[22] His hypothesis was a bold contradiction to the prevailing genetic theory. More recently however, twin studies have demonstrated that both environment and genetics play an important role in development.[23] Townsend et al., found that certain traits (tooth size and arch dimensions) are highly heritable, while others (intercuspal distance, overbite and overjet) had a stronger contribution from the environment.

Ambient Air Pollution and Respiratory Effects

Numerous studies have been done linking ambient air pollution to respiratory illnesses. Proximity to roadways and the subsequent pollution produced by motor vehicles has been shown in several studies to increase the severity and number of asthmatic episodes.[1,4,5,7] Traffic related pollution also increases the risk of atopic diseases and allergic sensitization.[2,8,9] Children are especially vulnerable to the effects of air pollution; their lungs are not fully developed, they generally have greater exposure than adults, and the exposure can deliver higher doses that may remain in the lungs for a greater duration.[6]

Air pollution also affects the development and function of the lungs. Expiratory flow and forced expiratory volume were both decreased in children exposed to higher levels of traffic-related air pollution.[3,11,12] Fanucchi et al.,[15] evaluated postnatal lung morphogenesis in infant monkeys, whose lung development is similar to humans. Airway morphology was evaluated at the end of 5 months of episodic exposure to 0.5 ppm ozone (O_3) and compared to a non-exposed control group. They discovered that episodic exposure to environmental O_3 compromised postnatal lung morphogenesis.

The effects of air pollution on the upper airway have also been analyzed. Wardas, et al., found that higher pollution levels increased the number of glycosaminoglycans (GAGs) in the palatine tonsils.[24] GAGs have been shown to increase the incidence of infections in the upper airway. The tonsils, even in a pristine environment, are host to numerous microbes vital to maintaining health. A disruption of the microbial flora by environmental air pollution, has been shown to increase the colonization of several facultatively pathogenic bacteria and fungi.[25]

Types of Air Pollution

Fine particles appear to have a greater effect on health for several reasons: (1) they remain airborne longer than large particles, increasing exposure time; (2) they have a larger surface to volume ratio, increasing their toxicity; and (3) they can lodge deeply in the lungs and even enter systemic circulation.[26] Motor vehicles, power plants, wood burning, and certain industrial processes are all sources of "fine" particulate matter (PM2.5), particles less than 2.5 micrometers in aerodynamic diameter. The United States Environmental Protection Agency (U.S. EPA) has issued a statement noting, "Health studies have shown a significant association between exposure to fine particles and premature death from heart or lung disease. Fine particles can aggravate heart and lung diseases and have been linked to effects such as: cardiovascular symptoms, cardiac arrhythmias, heart attack, respiratory symptoms, asthma attacks, and bronchitis."[26]

Other indicators of ambient air pollution are PM10 (particles less than 10 micrometers in aerodynamic diameter), ozone (O_3), nitrogen dioxides (NOx), and sulfur oxides (SOx). These are known as background or regional pollutants as they tend to distribute pervasively over wide areas, exhibiting large-scale variation, and the potential damage caused by them is experienced at locations removed from the source. In contrast, local pollutants are subject to small-scale variation and the potential harm caused by them is experienced near the source of emissions. It is important then, to distinguish the contributions of local and/or mobile sources of air pollution from background or regional sources. Local sources include stationary facilities or processes that generate a significant amount of air pollution during manufacturing, power generation, heating, etc. Mobile sources include on or off-road vehicles, cars, trains, boats, etc.[27] A commonly used

approach to estimating exposure to local and mobile emissions consists of measuring residential distance to stationary point sources (e.g., industrial plants), major roadways, and by characterizing traffic density near locations of interest (e.g., home, school, workplace, etc.).[6]

Geographic Information Systems

Recent studies have derived individual estimated exposure levels using geographic information systems (GIS)-based modeling. GIS is a system designed to capture, store, manage, manipulate, analyze, and present different types of geographically referenced data. The key advantage afforded by the use of GIS in health studies resides in the enhanced flexibility to link, integrate, process and query disparate data sets pertaining to environmental and health elements. A particularly significant advantage of the application of GIS technology in epidemiologic research is the possibility of flexibly geo-referencing the actual locations of subjects or patients and then seamlessly linking those locations with modeled exposure fields or specific sources.

Traditionally, data from the nearest air pollution monitoring site was used to estimate exposure using inverse distance methods. However, GIS provides the opportunity to implement sophisticated spatial models in order to predict pollutant concentration on a fine spatial scale, providing good approximations of long-term average exposures.[4] Scientists from longstanding air pollution epidemiologic studies (e.g., Loma Linda University's AHSMOG Study, Harvard's ACS Study, or University of Southern California's Children's Study) are now routinely using GIS-based methods for exposure assessment.

Employing GIS-based modeling techniques, Morgenstern et al.[2] recently identified a clear dose-response relationship for PM2.5 and sensitization to inhalant allergens. Other cohort studies of children living in southern California have discovered, using GIS modeling, that living within 500 meters of a freeway has resulted in significant deficits in lung function development.[5] In addition, living within 300 meters of arterial roads or freeways is associated with an increased risk of asthma-related repeated hospital encounters in children under the age of 18,1 while those who reside within 75 meters of a major road are at increased risk of being diagnosed with asthma.[4]

Effects on Craniofacial Morphology

Respiratory obstruction has been linked to changes in the craniofacial complex in many studies. Subjects with nasal breathing obstruction were found to have enlarged adenoids and a more vertical growth pattern.[27] A change in oral posture and the position of the tongue appear o be strong causative factors of a change in growth. Oral breathing necessitates that the tongue be in the floor of the mouth rather than the palate, altering the soft tissue muscular influence on both the maxillary and mandibular arches.[23] The absence of lateral force from the tongue in the palate allows the musculature of the cheeks to narrow the maxillary arch.[28] The resulting change in occlusion due to a narrow maxillary arch increases the vertical dimension.[18,28] The complete absence of nasal breathing has been shown to decrease mandibular length, nasal width, basilar length, intercuspal width, facial length, skull length, and cranial length.[29]

Treatment for nasal obstruction often includes removal of the adenoids, tonsils, or both. When the adenoids are removed due to obstruction, many subjects are able to

change to a nasal mode of breathing. These subjects also have a corresponding change in dentoalveolar height and a difference in ratio of upper and lower anterior face height.[30]

CHAPTER THREE

MATERIALS AND METHODS

Ethics and Confidentiality

This study was approved by the Institutional Review Board (IRB) of Loma Linda University. The orthodontists from each office gave written permission to use the collected protected health information (PHI). Data was anonymized from the data set and a random number was assigned to each subject prior to being geocoded by the GIS technician. Addresses were used solely for the purpose of calculating individual exposure to ambient air pollution and were removed from the data set prior to statistical analysis.

Cohort Data

Subjects for this study were randomly drawn from a sample of current and past patients from orthodontic offices in Santa Maria, CA (SM) and Upland, CA (UP) between the months of December 2011-February 2012. We used the Children's Health Study[32] to find two locations with highly contrasting air qualities. We found that SM was consistently at the lower end of air pollution metrics while UP was consistently at the higher end (Figure 1).

Inclusion criteria were: (1) adolescents aged 10-15, (2) having a diagnostic initial cephalometric radiograph. Exclusion criteria were: (1) individuals with previous orthodontic treatment and (2) craniofacial malformations or syndromes (e.g. cleft

lip/palate). Patients whose residential locations could not be geocoded due to incomplete or missing address information were also excluded.

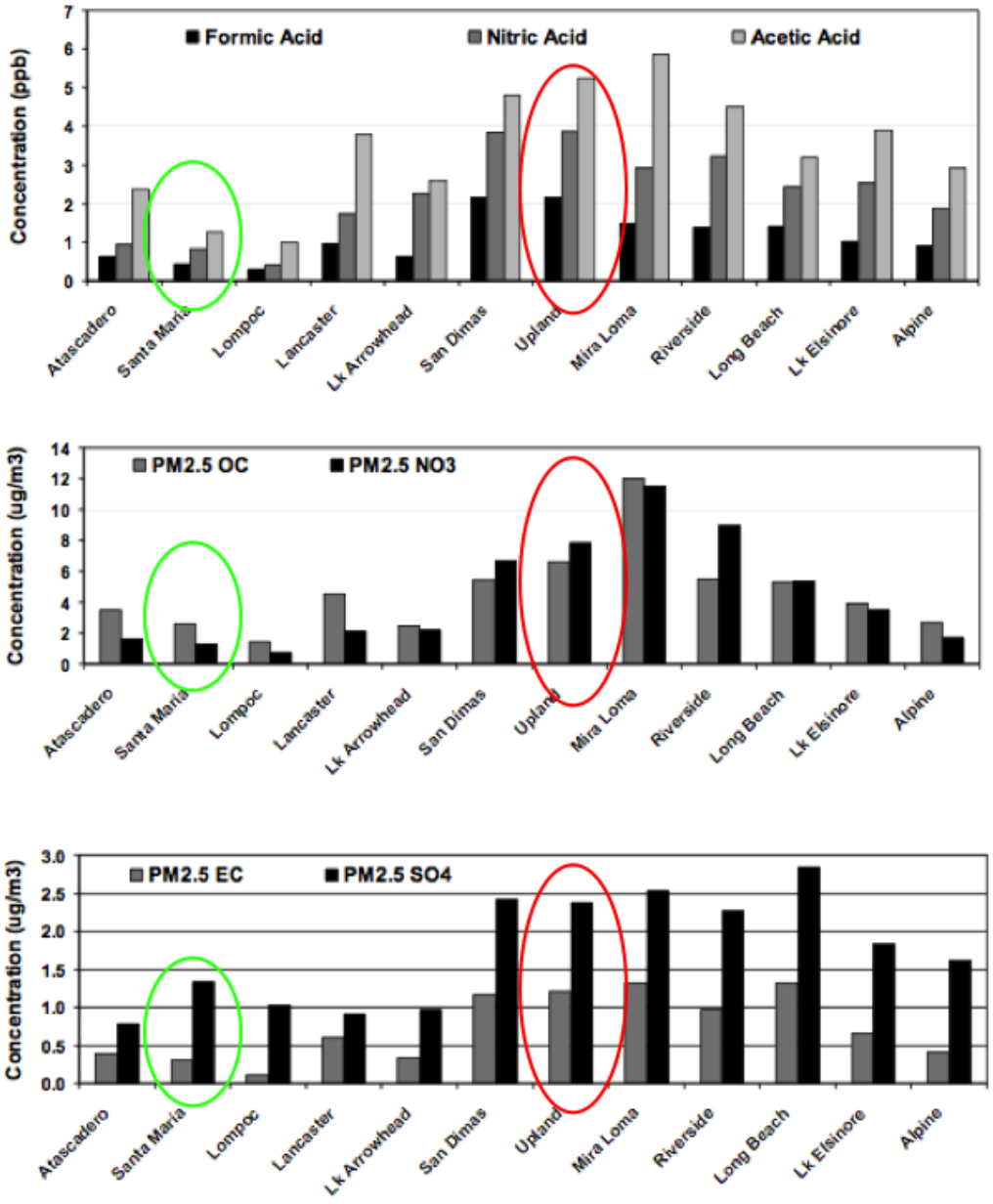

Figure 1. Figure taken from the Children's Health Study.[32] Upland (red ovals) had significantly higher levels of air pollution (taller bars) across multiple variables than Santa Maria (green ovals).

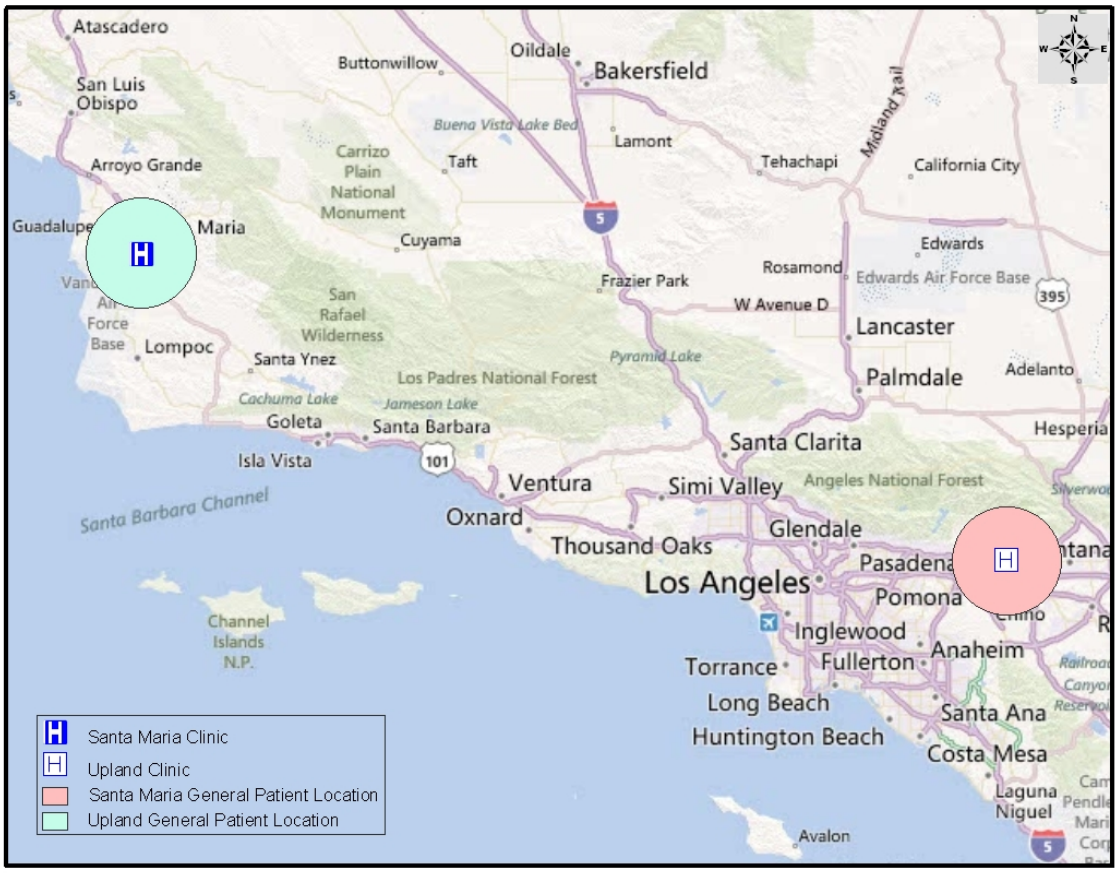

Figure 2. Map of study area and approximate locations of survey cohort. The letter "H" designates the location of each orthodontic office. The pink circle represents Upland and green circle Santa Maria.

Orthodontic Data Collection

Digital lateral cephalometric radiographs taken prior to the start of treatment were collected from orthodontic offices in Santa Maria, CA and Upland, CA (Figure 2). The Upland practice's radiographs were taken with a Planmeca ProMax imaging system using Dimax3 software. The Santa Maria office used a Yashida Kaycor system with Quick Ceph software. Collected digital radiographs from both locations were then imported and

traced with Quick Ceph Studio 3.0.7. The cephalometric measurements used (see Figure 3) were mandibular plane (MP-FH), facial axis (Na-Ba to PTV-Gn), facial depth (Na-Po to FH), lower face height (Xi-Pm to Xi-ANS) and total face height (Na-Ba to Xi-Pm).

All measurements were performed by one examiner. Angular measurements were made to the nearest 0.1 degree. Reliability of landmark identification was verified by repeating measurements on 80 randomly selected radiographs 5 months later. Measurements were recorded in a Microsoft Excel® 2007 spreadsheet.

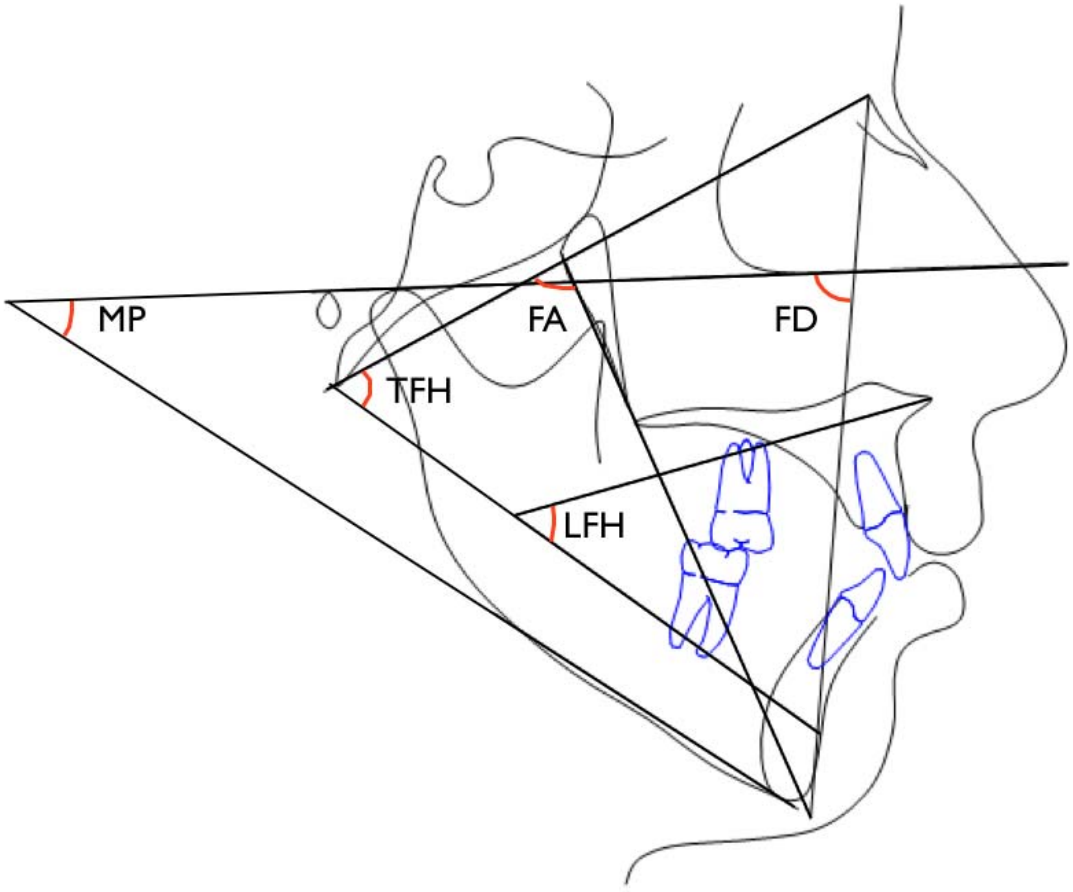

Figure 3. Cephalometric tracing showing the five craniofacial measurements used in this study to determine the growth pattern: Mandibular Plane (MP), Total Face Height (TFH), Facial Axis (FA), Lower Face Height (LFH), and Facial Depth (FD). Increased angles for MP, TFH, and LFH and decreased angles for FA and FD indicate a more vertical pattern.

Pollution Metrics

ArcGIS software (Esri Inc., www.esri.com), version 10.0 was used to geocode residential addresses obtained from patient chart information and to create several indicators of ambient air pollution exposure, accounting for background, local, and mobile sources (Table 1).

Table 1. .Summary of Pollution Metrics used to Characterize and Estimate Exposure of Subjects to Ambient Air Pollution

Pollution Metric	Definition	Units	Source
$PM_{2.5}$ (NAA, N24HA)	Exposure to particulate matter <2.5 µg in aerodynamic diameter compiled from data collected over 2009-2011.	Micrograms per cubic meter ($\mu g/m^3$)	Background
O_3 (EPDC, National 8-hour Average)	Ozone exposure, compiled from data collected over 2009-2011	Parts per million (ppm)	Background
Proximity to Toxic Waste Sources	Chemical exposure based on subjects' location within a 1-mile radius of a toxic waste site weighted for the ponds of toxic waste site weighted for the pounds of toxic waste emitted per year and the inhalation toxicity of chemical being released.	Pounds per square kilometer per year ($lbs/km^2/yr$)	Local
Road Density	The length of roads (in miles) that occur within a 1-mile radius of subjects' residence based on data from 2008.	Miles per square mile (mi/mi^2)	Local
Proximity to Traffic	Proximity values of 1,2,3 were given depending on if the residential distance was ≤ 100m, > 100m and ≤ 200m, or >200m respectively	Ordinal measure	Local

Background Air Pollution Sources

We estimated subjects' exposure to ambient air pollutants using data collected over the air quality monitoring network dispersed across southern California. GIS-derived geostatistical surfaces were linked with the subjects' residential and school locations in order to assign exposure estimates to each subject. All exploratory spatial data analyses, cross-validations, and spatial interpolations, were performed with the Geostatistical Analyst, a software extension available from ArcGIS 10.0. Exposure estimates were developed for the following air pollutants:

Particulate Matter 2.5 ($PM_{2.5}$)

To derive exposure assessments, we interpolated $PM_{2.5}$ data from the California Air Resources Board Air Quality System (http://www.arb.ca.gov/adam/index.html) and collected over 55 state and local district monitoring stations for the years 2009-2011. Two $PM_{2.5}$ metrics, anchored on the current National Ambient Air Quality Standards (NAAQS) framework, were developed: (1) the National Annual Average (NAA), and (2) the National High 24-Hour $PM_{2.5}$ Average (N24HA). The NAA for $PM_{2.5}$ is calculated based on the average of the year's quarterly averages. The N24HA captures extreme events and corresponds to the highest daily 24-hour $PM_{2.5}$ average observed in a given year. Both measures are used as a basis for federal designation of nonattainment areas. A given location is in violation of the NAA or the N24HA NAAQS if $PM_{2.5}$ concentrations exceed 15 or 65 micrograms per cubic meter, respectively.

A three-year average, 2009-2011, was computed for each $PM_{2.5}$ metric at each monitoring site. Two surfaces were then interpolated for each of the two PM metrics

using universal kriging (UK)(Figure 4) and a radial basis function (RBF) multiquadric interpolator (Figure 5).. Kriging interpolation, a stochastic method, tends to produce the best linear unbiased estimation of the air pollution field. However, after crossvalidation, following Jerret et al.,[31] a combination of UK and multiquadric RBF was used. This approach leverages the local detail in the RBF surface and the general trend in the UK surface. Estimated UK and RBF surfaces for the NAA and N24HA metrics were averaged based on 500-meter grid cells.

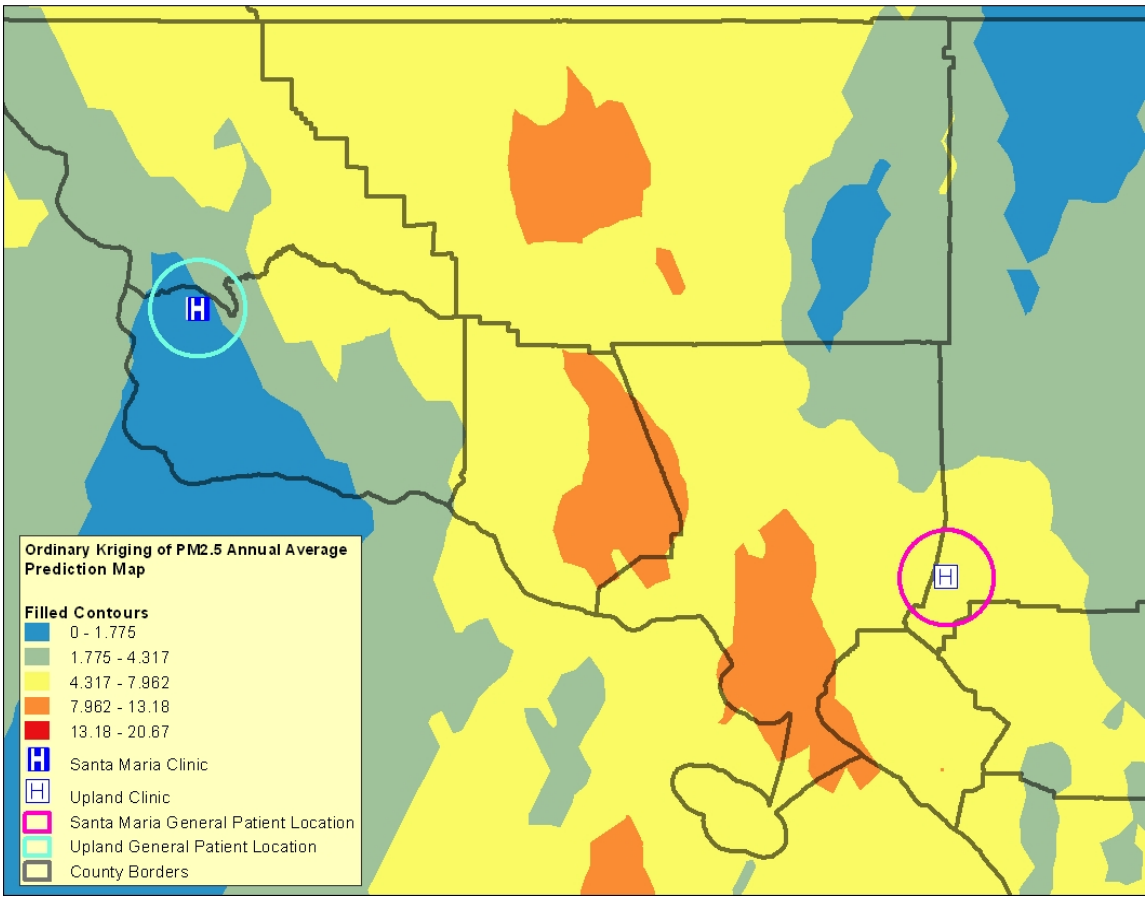

Fig 4. Map illustrating values of PM2.5 at each location compared to adjacent locations. The weight of the value decreases as the distance between points increases; ordinary kriging of National Annual Average (µg/m3) based on monitoring data collected over the years 2009-2011.

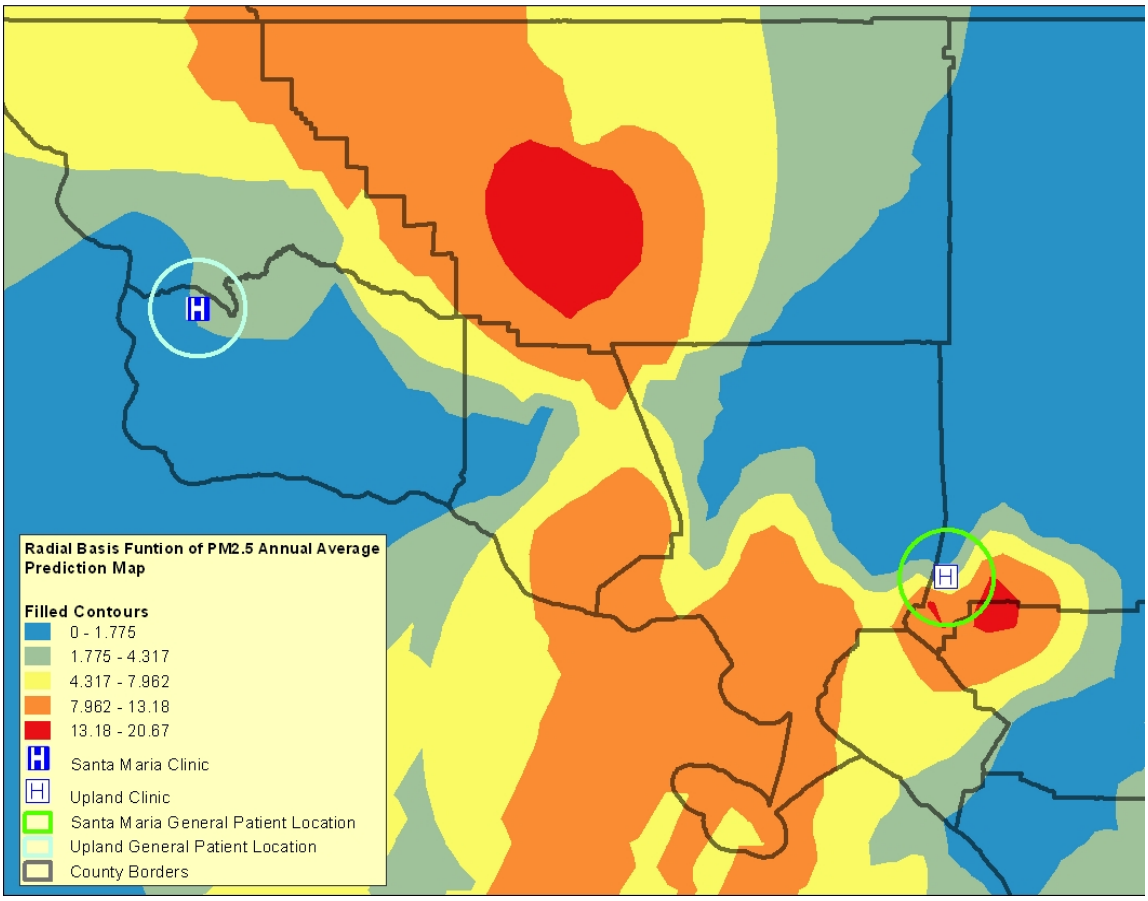

Fig 5. Map illustrating values of PM2.5 NAA (µg/m3) using Radial Basis Function (RBF). RBF surfaces are able to give better local detail than the general trend in the UK surface.

Ozone (O_3)

Like in the case of PM, two ozone indices were created based on the (NAAQS) framework: the expected peak daily concentration (EPDC) and National Ozone 8-Hour Design Value. O_3 data from the California Air Resources Board air quality database for 112 sites dispersed across the study area were also obtained. An ozone surface was interpolated using a UK exposure model based on the EPDC, which is a statistical measure designated to assess the likely exceedance of the 8-hour ozone average concentration at a given site based on the previous 3 years. The EPDC captures extreme events and represents a robust index for estimating stable spatial patterns of likely ozone exceedances. Year-specific EPDC values at each monitoring station were estimated for the period 2009-2011 and then interpolated. In addition, an ozone exposure surface was derived via UK based on the national 8-hour design value. This metric represents the average of the three annual fourth highest 8-hour averages over 2009-2011. The national 8-hour standard is violated when the national 8-hour ozone design value is greater than or equal to 0.075 ppm.

Local Stationary Sources

Proximity to Toxic Waste Sources

Data on local exposures to hazardous waste and other sources of air toxics were obtained form Toxic Release Inventory (TRI) for 2010 (Figure 6). The TRI database is maintained by the US EPA and contains information on the quantity of certain chemicals released into the environment by toxic waste facilities in the U.S. While the TRI database only includes large facilities, it does give a reasonable approximation of the

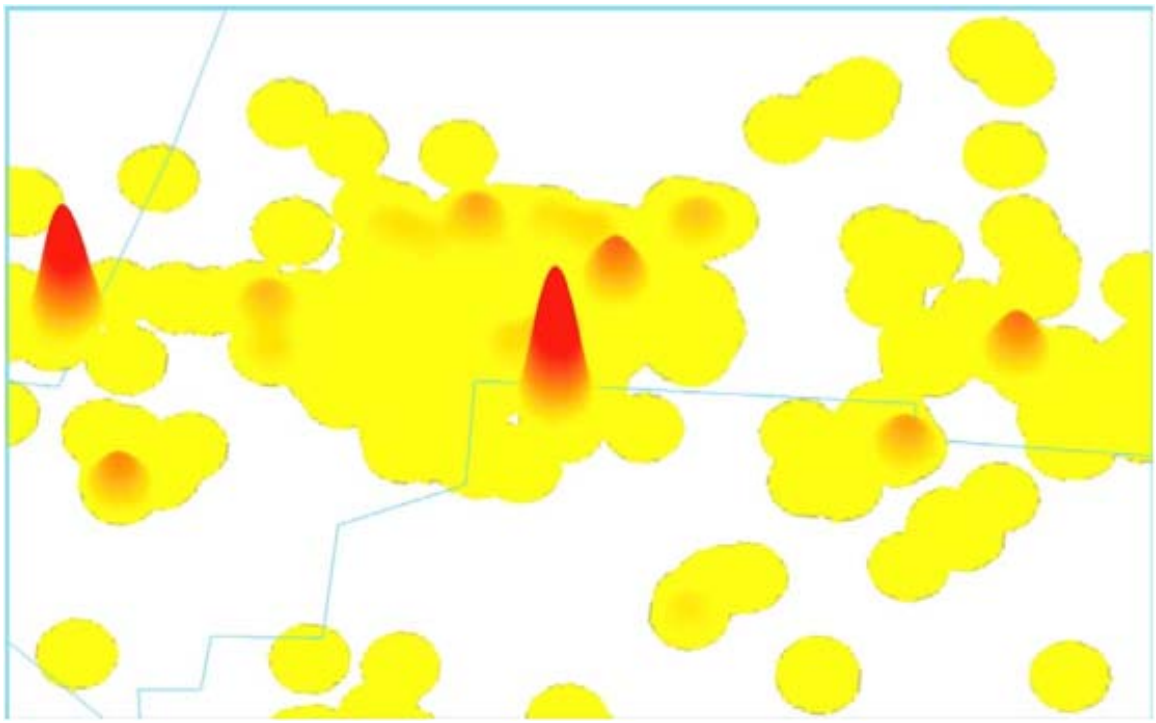

Fig 6. Example of map used to determine exposure to local sources of toxic waste modeled by applying a 1-mile kernel density function to EPA's Toxic Release Inventory dataSites. Blue lines delineate counties. Each circle represents a 1-mile radius around each toxic waste site with the facility located at the center. A color gradient from yellow to red indicates the amount of exposure to toxins, with the darker red representing greatest exposure. In addition, the taller the cone, the greater the exposure.

amount of such activity in a neighborhood. The air pollution metric created was the pounds of toxic waste emitted per year, weighted by the inhalation toxicity of each particular chemical. Briefly, the procedure for creating this measure is as follows. First, the location of each site was geocoded according to the EPA supplied coordinates. Second,a measure was developed that aggregated the emissions by TRI location, taking into account the toxicity of the particular chemicals being released by multiplying the pounds of each chemical released by a unique inhalation toxicity score using the Risk-Screening Environmental Indicators tool constructed by the U.S. EPA (see **http://www.epa.gov/opptintr/rsei** for more information on the RSEIs tool). Third, a

kernel density function (KDF) implementing a one-mile radius neighborhood was applied to the set of TRI locations operating a given year to model the area impacted by the toxic waste released from each site. In this manner, a KDF-based surface was produced for the TRI data were available. Although the area impacted by toxic waste varies according to the chemical involved and local meteorology, a KDF based on one-mile neighborhoods was chosen since this distance has been validated as a reasonable approximation of the geographic dispersion of the impact from these sources. Prior studies proceed by apportioning the estimated amount of toxic waste to the exposed populations near the TRI facilities under the assumption that the concentration of the emitted chemicals is constant within the one- mile buffer defined around each site. The KDF however more realistically models the dispersion of pollutants away from the source as it is a distance-decay function which produces an exposure field (or virtual landscape) across which emissions peak at the top of a series of bell-shaped domains centered at the exact locations of the TRI facilities. This gradually decreases within one mile around each site, and drops to zero beyond that distance.

Finally, the KDF yearly surface was overlaid with the GIS layers representing the residential locations of the patients in order to assign the exposures related to the emissions from TRI facilities located within one mile of the home and school locations. In regions where TRI sites were in close proximity, the amounts of toxic waste modeled through the KDF were summed up at locations where the one-mile neighborhoods around each facility overlapped. This ensured that subjects who reside at points located under two (or more) KDF-derived toxic waste bell-shaped domains are assigned exposure estimates based on the impact of all of the facilities found within one mile of home and

school locations. The total annual exposure estimates were divided by 12 to arrive at an "average" monthly value. For each patient, the total exposure resulted from cumulating the average monthly exposure estimate over age calculated in months.

Mobile Sources

To assess the impact of local traffic, two metrics were constructed: road density (RD) and proximity to traffic (TP). RD approximates the density of the transportation network near residential and school locations, while TP provides an estimate of the residence's proximity to major roadways. In other words, RD assesses the number of roads near the patient, while TP quantifies how close those roads are.

It is assumed that patients who live near busy roads experience greater exposure to traffic-related emissions, compared to those who live further away. RD and TP approximated exposure to traffic pollution, which may exert independent effects in addition to pollutants such as $PM_{2.5}$ and O_3, which vary over larger areas.

Road Density (RD)

Freeways and major roads were identified according to the U.S. Bureau of the Census feature class codes, and extracted from a GIS database (i.e. Streetmap, which is based on commercial street data from NAVTEQ and Tele Atlas/TomTom for the United States, www.Esri.com/data/streetmap). Using GIS-based geoprocessing tools, the total length (in miles) of all major road segments within a 1-mile radius of residential and school locations was summed and this value was then assigned to each patient.

Proximity to Traffic (TP)

Residential traffic proximity was characterized for major roadways. Three indicators of roadway proximity were evaluated through a three-tiered exposure gradient: a) ≤ 100 m; b) > 100 m and ≤ 200 m; and c) > 200 m. The areas within 100 m or 200 m of either side of a major road are referred to as 100-m and 200-m buffers. Patients were assigned proximity indicators 1, 2, or 3 if their geocoded residential locations fell within the 100-m buffer, the 200-m buffer, or occurred beyond 200 m, respectively.

Statistical Analysis

The craniofacial measurement and air pollution data was exported from the Microsoft Excel 2007 spreadsheet and imported into the SAS v. 9.2 and SPSS v. 19.0 (IBM corporation) software packages for statistical analysis. Standard descriptive statistics (means and standard deviations) were calculated for all measurements. A p-value of $\alpha < 0.05$ was considered statistically significant.

Reliability of angular measurements was evaluated using Cronbach's alpha and intraclass correlation. Measurements were repeated on 10% of the subjects (n=80) with an interval of 5 months between measurements. A Cronbach's alpha of 0.8 to 1.0 was considered a strong correlation.

This was a cross-sectional study design. Given that the sets of dependent variables (FA, MP, FD, LFH, TFH) and independent variables (PM2.5, O3, and other pollution metrics) were measured on a continuous scale and contained data not normally distributed, statistical analysis included Spearman's rho.

CHAPTER FOUR

RESULTS

Study Population

The study population consisted of 764 subjects. 372 came from the Santa Maria clinic (SM), while 392 came from the Upland (UP) clinic. 807 subjects were originally included in the study, but 43 were excluded due to either unreadable radiographs or unusable addresses (P.O. Box or out of state address). All the subjects were between the ages of 10-15 years old. The SM group averaged an age of 12.7 years, while the UP group averaged 12.2. The mean of the entire sample was 12.5 years We were unable to record other demographic data. Table 2 illustrates some of the demographic differences between SM and UP.

Table 2. Demographic data from the Children's Health Study illustrating some of the differences between the two communities.[32] Racial makeup and income differ significantly.

Community	Eligible Subjects	Subjects with Baseline Questionnaire Information (%)		White	Black	Asian	Other	Hispanic	Male	Income > $50,000
Alpine	396	298	(75)	84.0	0.4	0.8	14.8	12.8	49.8	37.5
Atascadero	371	260	(70)	84.1	0.4	0.4	15.1	11.4	40.5	36.3
Lake Elsinore	397	316	(80)	76.9	2.3	1.7	19.1	23.8	53.1	25.6
Lake Arrowhead	402	347	(86)	83.8	0.6	1.5	14.1	16.2	48.5	36.3
Lancaster	350	266	(76)	70.4	5.8	2.5	21.3	26.8	45.7	29.4
Lompoc	410	305	(74)	72.5	8.7	0.8	18.0	19.3	50.0	32.6
Long Beach	414	325	(79)	37.9	16.1	21.8	24.2	22.3	47.9	31.1
Mira Loma	438	308	(70)	66.8	1.1	1.4	30.7	34.0	46.3	29.4
Riverside	469	369	(79)	43.9	14.0	6.4	35.7	38.4	47.1	21.4
San Dimas	397	303	(76)	61.6	5.8	8.8	23.8	29.7	47.8	34.3
Santa Maria	371	300	(81)	46.3	1.6	2.8	49.3	60.1	48.1	12.9
Upland	428	279	(65)	69.4	2.6	8.7	19.3	16.7	49.6	65.6
Total	4,843	3,676	(76)	66.1%	5.1%	4.9%	23.9%	26.0%	47.9%	32.2%

Craniofacial Measurements

Each of the craniofacial indicators followed a normal distribution pattern (Figure 7). FD was the only measurement that had a median that was significantly different ($\alpha < 0.05$) between UP and SM ($\alpha = 0.042$).

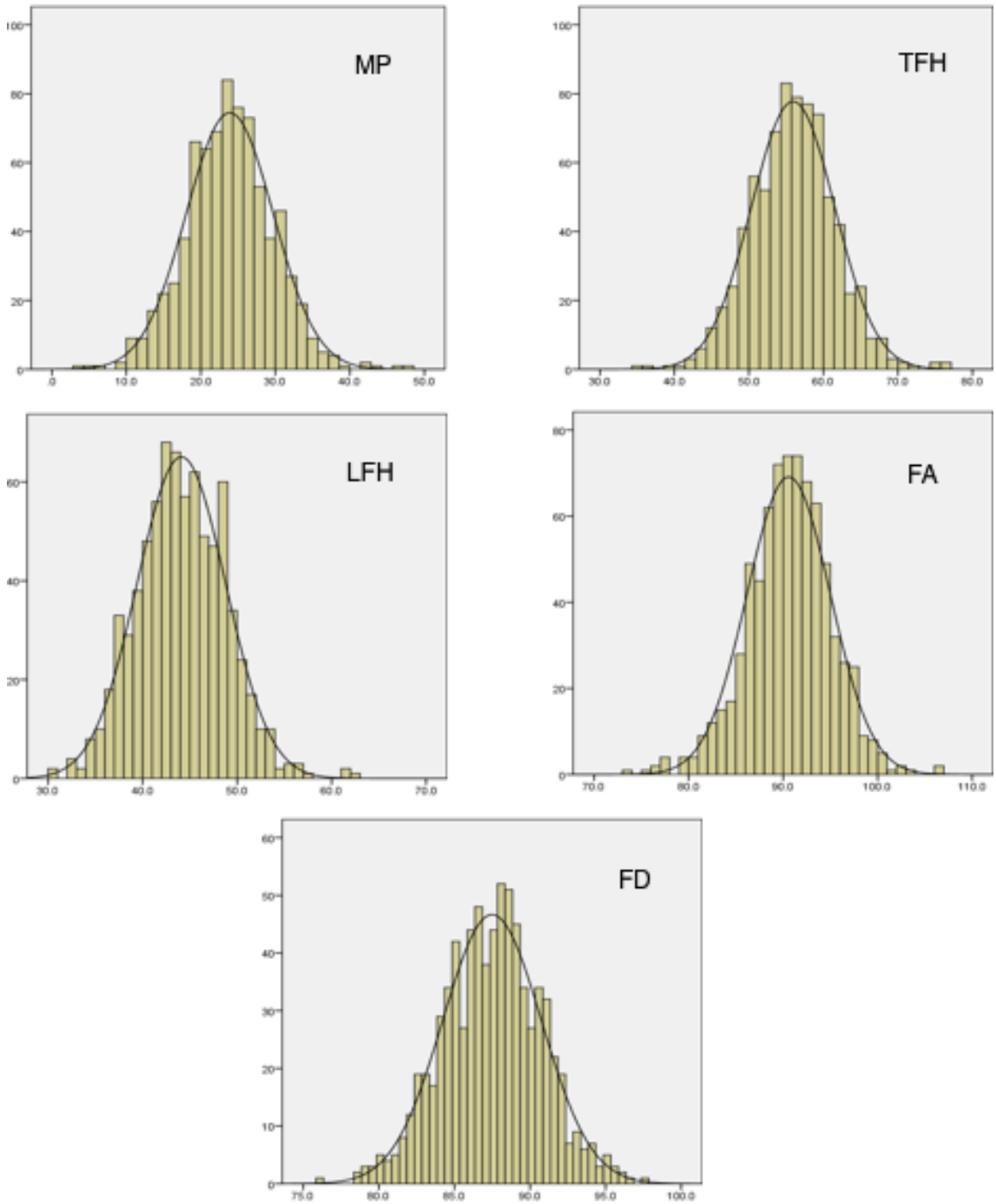

Figure 7. Histograms showing the distribution of each of the craniofacial measurements. Mandibular Plane (MP), Total Face Height (TFH), Lower Face Height (LFH), Facial Axis (FA), and Facial Depth (FD) each followed a normal distribution. The y axis represents the number of patients and the x axis represents the craniofacial measurement in degrees.

All of the craniofacial measurements trended toward a more brachyfacial pattern and had a larger standard deviation when compared to published Caucasian norms (Table 3). The measurement difference could be due to racial variability in norms. Larger standard deviations are probably due to differences in sample size. Comparing the averages of the two cohorts indicate similar results, with the means only varying between .1-.6 degrees (Table 4).

Table 3. Craniofacial Caucasian norms compared to observed means with standard deviations. The observed measurements all indicate a less vertical pattern than the published norms.

Craniofacial Indicator	Caucasian Norm	Norm Std. Dev.	Observed	Observed Std. Dev.
MP	26	± 4	23.9	± 5.8
TFH	60	± 3	55.9	± 5.6
FD	87	± 3	87.5	± 3.3
LFH	45	± 4	44.1	± 4.7
FA	90	± 3	90.6	± 4.4

Table 4. Baseline Characteristics of Craniofacial Data

Craniofacial Measurement		Santa Maria	Upland
Mandibular Plane	Mean	23.6	24.2
	Standard Deviation	6.1	5.6
	Median	23.7	24.1
	Percentile 25	19.5	20.3
	Percentile 75	27.2	27.8
	Minimum	3.7	5.5
	Maximum	48.4	42.9
Total Face Height	Mean	55.6	56.2
	Standard Deviation	5.8	5.4
	Median	55.8	56.2
	Percentile 25	52.2	52.6
	Percentile 75	58.9	59.7
	Minimum	35.7	39.0
	Maximum	76.9	76.0
Facial Depth	Mean	87.3	87.7
	Standard Deviation	3.3	3.2
	Median	87.4	87.9
	Percentile 25	85.0	85.3
	Percentile 75	89.6	89.9
	Minimum	76.1	79.7
	Maximum	97.7	96.4
Lower Face Height	Mean	44.1	44.0
	Standard Deviation	4.7	4.6
	Median	44.0	43.9
	Percentile 25	41.1	40.8
	Percentile 75	47.4	47.4
	Minimum	30.7	30.8
	Maximum	62.8	61.9
Facial Axis	Mean	90.6	90.5
	Standard Deviation	4.7	4.2
	Median	90.8	90.7
	Percentile 25	88.0	87.7
	Percentile 75	93.4	93.4
	Minimum	73.9	75.0
	Maximum	106.8	103.5

Air Pollution Metrics

The air pollution data showed a significant difference ($\alpha < 0.05$) in levels of O_3 ($\alpha = 0.000$) and $PM_{2.5}$ ($\alpha = 0.000$) between the Upland and Santa Maria cohorts. TRI ($\alpha = 0.601$) and RD ($\alpha = 0.731$) were not significantly different (Table 5).

Table 5. Baseline Characteristics of Air Pollution Data

Air Pollution Measurement		Santa Maria	Upland
Total Exposure (TRI)	Mean	156	87
	Standard Deviation	1385	872
	Median	0	0
	Percentile 25	0	0
	Percentile 75	0	0
	Minimum	0	0
	Maximum	17006	14702
Road Density	Mean	2.5	0.4
	Standard Deviation	15.3	1.7
	Median	0.0	0.0
	Percentile 25	0.0	0.0
	Percentile 75	0.0	0.0
	Minimum	0.0	0.0
	Maximum	202.6	10.2
Ozone EPDC	Mean	0.083730	0.105439
	Standard Deviation	0.002031	0.004248
	Median	0.084564	0.105777
	Percentile 25	0.083102	0.103561
	Percentile 75	0.084564	0.108462
	Minimum	0.060250	0.065638
	Maximum	0.100472	0.113313
Ozone 8-Hour Average	Mean	0.127250	33.216373
	Standard Deviation	1.011048	9.039733
	Median	0.069014	33.387869
	Percentile 25	0.031319	28.860487
	Percentile 75	0.120561	38.042360
	Minimum	-0.036782	-0.019013
	Maximum	19.492577	64.527178

$PM_{2.5}$ 24- Hour Average	Mean	0.4300320	2.7707969
	Standard Deviation	0.3963550	1.1114654
	Median	0.3688308	2.4665893
	Percentile 25	0.3486995	1.9149755
	Percentile 75	0.4509595	3.5214795
	Minimum	0.2562955	0.3289260
	Maximum	7.6895180	6.1260770
$PM_{2.5}$ Annual Average	Mean	1.636466	5.939368
	Standard Deviation	0.720385	2.174495
	Median	1.608065	5.229509
	Percentile 25	1.262535	4.186914
	Percentile 75	1.844260	7.689039
	Minimum	0.408861	1.176681
	Maximum	9.003932	11.797426

The distributions of both PM2.5 and O3 were clearly separated by location (Figures 8, 9). For both histograms the spike on the left represents the Santa Maria cohort, while the spike on the right represents Upland.

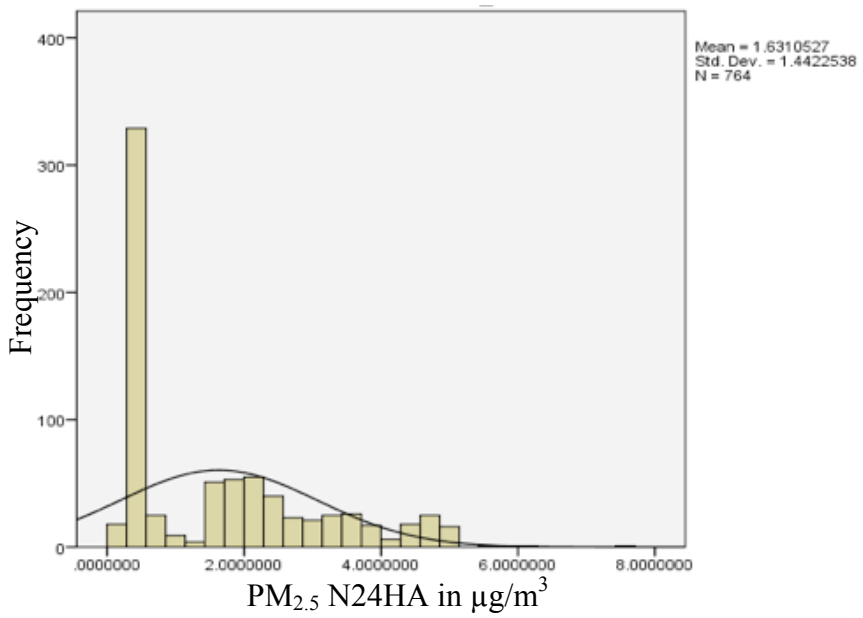

Fig 8. Histogram depicting $PM_{2.5}$ Predicted 24 Hour Average for the entire patient population. The peak to the left represents SM, while the group to the right represents UP. The separate grouping shows a clear difference in $PM_{2.5}$ levels between the sample areas.

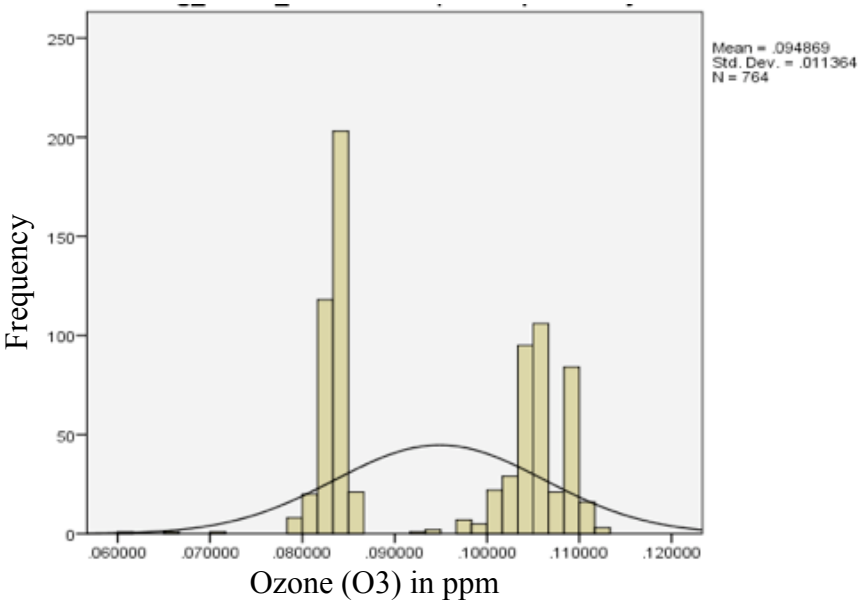

Fig 9. Histogram depicting O_3 exposure for the entire patient population study population. The peak to the left represents SM, while the group to the right represents UP. The clear bimodal distribution indicates a significant difference in O_3 exposure between the sample areas.

Reliability

The coefficients of Cronbach's alpha and intraclass correlation (ICC) are shown in Table 6, demonstrating high reliability for the five cephalometric measurements with narrow confidence intervals in all measurements except total face height. The lower bound of TFH shows a high correlation, but low agreement. The measurements were consistently higher than the originals for the 80 random subjects selected for reliability testing.

Table 6. Reliability: Cronbach's Alpha and Intraclass Correlation. Both show high reliability, however the lower bound of the 95% confidence interval for TFH showed poor agreement.

Craniofacial Measurement	Cronbach's Alpha	ICC	95% Confidence Interval	
			Lower Bound	Upper Bound
MP	0.973	0.974	0.959	0.983
TFH	0.974	0.931	0.231	0.980
FD	0.970	0.964	0.927	0.980
LFH	0.969	0.953	0.838	0.980
FA	0.973	0.961	0.868	0.983

Spearman's Rho Correlation

Spearman's rho correlation coefficient was used to assess the correlation between air pollution metrics and craniofacial measurements. We chose the non-parametric Spearman's rho due to the fact that some of our air pollution data (RD and RP) were ordinal data and not normally distributed.

Between craniofacial measurements and air pollution data no statistically significant correlation was found (Table 7). Within the air pollution data, however, there was a strong correlation between $PM_{2.5}$ 24HA, $PM_{2.5}$ AA, and O_3. RD and RP also correlated with each other. A strong correlation between the air pollution metrics was expected since many of the sources of ambient air pollution produce multiple types of pollution. A strong correlation between RD and RP also is expected since areas with a higher density of roads will tend to have residences in closer proximity.

Table 7. Spearman's Rho: Correlations between Air Pollution Metrics and Craniofacial Measurements

Variable	TRI	RD	RP	EPDC	$PM_{2.5}$ 24HA	$PM_{2.5}$ AA	O3
MP							
Correlation	.083*	-0.015	0.003	0.041	0.030	0.056	.071*
Sig. (2-tailed)	0.021	0.682	0.928	0.257	0.408	0.121	0.048
TFH							
Correlation	0.059	-0.022	0.017	0.045	0.028	0.058	0.059
Sig. (2-tailed)	0.102	0.536	0.630	0.216	0.432	0.111	0.102
FD							
Correlation	-.078*	0.031	0.004	0.057	0.066	0.058	0.034
Sig. (2-tailed)	0.031	0.398	0.903	0.114	0.068	0.107	0.354
LFH							
Correlation	.073*	-0.006	0.010	0.001	-0.037	0.008	0.011
Sig. (2-tailed)	0.045	0.877	0.786	0.988	0.312	0.818	0.769
FA							
Correlation	-0.063	0.037	-0.034	-0.035	0.001	-0.035	-0.032
Sig. (2-tailed)	0.080	0.310	0.344	0.341	0.979	0.329	0.376
TRI							
Correlation	1	-0.021	0.024	0.059	-.082*	0.024	0.030
Sig. (2-tailed)		0.560	0.511	0.101	0.024	0.515	0.403
RD							
Correlation	-0.021	1	-.888**	-0.058	0.002	-0.017	-0.049
Sig. (2-tailed)	0.560		0.000	0.109	0.947	0.644	0.173
Proximity							
Correlation	0.024	-.888**	1	0.063	-0.001	0.021	0.059
Sig. (2-tailed)	0.511	0.000		0.079	0.979	0.556	0.101
EPDC							
Correlation	0.059	-0.058	0.063	1	.724**	.747**	.819**
Sig. (2-tailed)	0.101	0.109	0.079		0.000	0.000	0.000
PM2.5 24HA							
Correlation	-.082*	0.002	-0.001	.724**	1	.906**	.692**
Sig. (2-tailed)	0.024	0.947	0.979	0.000		0.000	0.000
PM2.5 AA							
Correlation	0.024	-0.017	0.021	.747**	.906**	1	.721**
Sig. (2-tailed)	0.515	0.644	0.556	0.000	0.000		0.000
O3							
Correlation	0.030	-0.049	0.059	.819**	.692**	.721**	1
Sig. (2-tailed)	0.403	0.173	0.101	0.000	0.000	0.000	

*Correlation is significant at the 0.05 level (2-tailed).

**Correlation is significant at the 0.01 level (2-tailed).

CHAPTER FIVE

DISCUSSION

Our study was a follow up to the research done by Kaplan.[20] She examined differences in craniofacial morphology and dental malocclusion in relation to ambient air pollution. We attempted to simplify and strengthen her study by focusing only on craniofacial morphology, selecting two heterogenous air pollution environments, and significantly increasing the sample size. The Children's Health Study has established air quality measurements from communities throughout Southern California. We chose Santa Maria and Upland because of their contrasting air qualities.

Statistical Significance

No statistically significant correlation between the air pollution metrics and the craniofacial measurements were found. There was no significant difference between the craniofacial measurements of each sampling area, with the exception of a small difference in the medians of facial depth. The air pollution metrics between the two sampling areas were, however, significantly different.

Clinical Significance

In order to have a clinically significant change, our outcome variables would need to change by at least several degrees. What we instead found was that the means between

groups only varied from .1-.6 degrees. Such a small change in any of the measurements would not be likely to change the diagnosis or treatment planning of any subjects. The small variation is well within the expected error inherent to tracing the radiographs.

Strengths and Weaknesses

The study has several strengths. First, we were able to identify two areas in Southern California with highly contrasting air qualities. The Children's Health Study[32] indicated that Upland and Santa Maria have some of the highest and lowest levels of air pollution respectively and our data confirmed that. Second, our sample size of roughly 800 subjects is more than adequate for a study of this nature. And third, we used multiple craniofacial measurements to measure vertical growth. FA, TFH, FD, and MP all incorporate some portion of the cranial base, while LFH uses the maxilla and mandible. If there was a significant change in vertical growth, one of these measurements should have been able to detect it.

The major weaknesses of this study were mostly related to the huge number of confounding variables that we were unable to account for. Sex, race, residential history, history of household smoking, indoor/outdoor time, diet, full medical history, etc., were not included in our data. Acquiring this data requires a comprehensive questionnaire, which would be time prohibitive for us when conducted on groups of this size.

Also, our study was only able to look at one of the final adaptive changes to an environmental stimulant. The chain of events that lead to a change in craniofacial morphology is long. We didn't measure or detect any of the intermediate stages (change in posture, decrease in airway volume, change in mode of breathing, etc.). Being able to

see the progression of physiological and anatomical adaptation in response to a higher level of air pollution could have helped isolate causative variables along the way.

Areas for Further Study

In order to find any correlations in this type of study, the many confounding variables need to be accounted for. Further studies need to either have a comprehensive questionnaire along with a large sample size or use an established cohort, such as from the USC Children's Health Study.[32]

What may prove most beneficial is studying correlations between air pollution and the many adaptive changes that occur before craniofacial morphology changes. Airway volume, airflow, postural changes, and mode of breathing should be affected prior to the subject having an adaptation in vertical facial growth. Future studies should incorporate exhaustive patient histories with the aforementioned indicators of adaptation.

Conclusions

The null hypothesis was accepted and no association between ambient air pollution and craniofacial measurements was found..

1. Using two areas with contrasting levels of air pollution offers a distinct advantage with exposure studies. Future studies should attempt to maximize the difference between the sample areas.

2. Growth of the craniofacial complex depends on a large number of variables. Accounting for these many variables is difficult, but necessary to isolate contributing factors.

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